

WHAT IS CLAIMED IS:

1. A method for identifying a drug lead compound that binds to a target biological molecule (TBM) of interest, the method comprising:

(a) assembling a library of candidate target binding fragments (CTBF) capable of being chemically cross-linked by a cross-linker to provide candidate cross-linked target binding fragments for binding to the target biological molecule;

(b) screening the library of candidate target binding fragments to identify at least first and second candidate target binding fragments that bind to the target biological molecule;

(c) chemically cross-linking the at least first and second candidate target binding fragments or structurally related analogs thereof with a cross-linker to provide a library of candidate cross-linked target binding fragments for binding to the target biological molecule; and

(d) screening the library obtained in (c) to identify a drug lead compound that binds to the target biological molecule.

2. The method according to Claim 1, wherein at least one of the candidate target binding fragments of the library of candidate target binding fragments binds to the target biological molecule with a K_d of from about 5 mM to about 0.05 mM.

3. The method according to Claim 1, wherein at least one of the candidate target binding fragments of the library of candidate target binding fragments binds to the target biological molecule with a K_d of from about 3 mM to about 0.1 mM.

4. The method according to Claim 1, wherein the drug lead compound identified in step (d) binds to the target biological molecule with a K_d of 500 nM or lower.

5. The method according to Claim 1, wherein the screening steps (b) and (c) consist essentially of an *in vitro* biological assay.

6. The method according to Claim 1, wherein the library of candidate cross-linked target binding fragments for binding to the target biological molecule comprises homodimeric or heterodimeric candidate cross-linked target binding fragments.

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7. The method according to Claim 1, wherein the library of candidate target binding fragments comprises candidate target binding fragments of less than about 500 daltons.

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8. The method according to Claim 1 wherein the library of candidate cross-linked target binding fragments comprises candidate cross-linked target binding fragments of less than about 750 daltons.

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9. The method according to Claim 1, wherein the target biological molecule is a human or human pathogen protein.

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10. The method according to Claim 9, wherein the protein is an enzyme, a human hormone, a human receptor and fragments thereof having nitrogen's in the protein present in their naturally occurring isotopic abundance.

11. The method according to Claim 1, wherein at least one of the screening steps (b) and (d) is accomplished by ELISA assay.

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12. A method for inhibiting the binding of a first biological molecule to a second biological molecule that binds to the first biological molecule, the method comprising:

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contacting a system comprising both the first and second biological molecules with a binding inhibitory amount of a drug lead compound identified according to the method of Claim 1, wherein the drug lead compound binds to the first biological molecule and inhibits its ability to bind to the second biological molecule.

13. The method according to Claim 12, wherein the first and second biological molecules are human proteins.

14. The method according to Claim 13, wherein the first and second biological molecules are selected from the group; a human hormone, cytokine or chemokine, a human receptor and fragments thereof

15. A method for identifying a drug lead compound that binds to a target biological molecule of interest, the method comprising:

- 10 (a) assembling a library of candidate target binding fragments, each fragment containing an oxime linking group;
- (b) screening the library of candidate target binding fragments or monomers to identify at least first and second oxime containing candidate target binding fragments that bind to the target biological molecule;
- 15 (c) chemically crosslinking the aldehyde analogs of the at least first and second oxime containing candidate target binding fragments with an O,O'-diamino-alkanediol cross-linker to provide a library of oxime containing candidate cross-linked target binding fragments for binding to the target biological molecule; and
- (d) screening the library obtained in (c) to identify a drug lead compound
- 20 that binds to the target biological molecule.

16. A method comprising:

- (a) assembling a library of candidate target binding fragments (CTBF), each fragment having a linkable functional group (LFG) or blocked form thereof (BLFG), the blocked form containing a linking group (LG);
- 25 (b) contacting the candidate target binding fragments with a target biological molecule (TBM);
- (c) measuring a change in a first physical association (PA-1) of the target biological molecule;
- 30 (d) selecting target binding fragments (TBF) based on (c);
- (e) reacting selected target binding fragments having a linkable functional group with a cross-linker, having chemically compatible cross-reactive groups (CFG)

with the LFG, under conditions suitable for forming a library of candidate cross-linked target binding fragments (CXL-TBF);

(f) contacting the candidate cross-linked target binding fragments with the target biological molecule (TBM);

5 (g) measuring a change in a second physical association (PA-2) of the target biological molecule;

(h) selecting cross-linked target binding fragments (XL-TBF) based on (g).

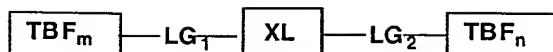
10 17. The method of Claim 16 wherein the candidate target binding fragment contacted with the TBM contains a blocked linkage functional group (BLFG) containing linking group LG.

15 18. The method of Claim 17 where in the linking group (LG) in BLFG is selected from the group; oxime, hydrazone, N-acyl hydrazone, secondary amine, tertiary amine, acetal, ketal, 1,2 amino alcohols, amide, N,N-disubstituted amides, thioamide, ureido, thioureido, carbamate, thiocarbamate, thiothiocarbamate, sulfonamide, carbonate, guanidino, amidino, thioester, ester, ether, 2-hydroxyether, 2-hydroxythioether, thioether, disulfide, alkane (alkylene), alkene (alkenylene) and alkyne (alkynylene).

20 19. The method of Claim 18 wherein each candidate target binding fragment (CTBF) of step (b) contains the same linking group (LG) as is present in the candidate cross-linked target binding fragment (CXL-TBF) of step (f).

25 20. The method of Claim 19 wherein the linking group (LG) is selected from the group; oxime, secondary amine, tertiary amine, amide, ureido, thioureido, sulfonamide and carbamate.

30 21. The method of Claim 19 wherein two candidate target binding fragments (CTBF) selected from step (d) are cross-linked to form a candidate cross-linked target binding fragment (CXL-TBF) represented by



where

5 TBF_m is a first TBF selected from step (d) which contained LG_1 in its blocked linking group ;

TBF_n is a second TBF selected from step (d) which contained LG_2 in its blocked linking group;

XL represents the cross-linker without the chemically compatible cross-reactive functional groups;

10 LG_1 represents the linking group in the first TBF; and

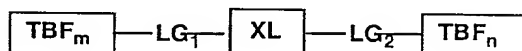
LG_2 represents the linking group in the second TBF.

22. The method of Claim 21 wherein LG_1 and LG_2 are the same or are different and are selected from the group oxime, secondary amine, tertiary amine, amide, ureido, thioureido, sulfonamide and carbamate.

23. The method of Claim 21 wherein TBF_m and TBF_n are the same or are different.

20 23. The method of Claim 21 where XL is selected from the group of alkanes: methylene, ethylene, propylene, butylene, pentylene, hexylene and heptylene, optionally containing 0, 1, 2 or 3 ether linkages and from 1-3 double bonds and aryls: ortho-, meta- or para- $\text{C}_6\text{-C}_6$ -alkyl-phenyl- $\text{C}_6\text{-C}_6$ -alkylene .

25 24. The method of Claim 16 wherein the candidate cross-linked target binding fragments are represented by the formula:



30 where

TBF_m represents a first TBF selected from step (d);

TBF_n represents a second TBF selected from step (d);

XL represents the cross-linker without the chemically compatible cross-reactive functional groups selected from the group

C₀-C₁₀-alkylene,
C₀-C₆-alkyl-C₆-C₁₀-aryl-C₀-C₆-alkylene,
C₁-C₆-alkyl-N(R₁)-C₁-C₆-alkylene,
(C₁-C₆-alkyl-O-C₁-C₆-alkylene)_n, where n=1, 2, 3 or 4;

LG₁ and LG₂ are linking groups independently selected from the group

-C(R_a)=N-O-, -O-N=C(R_a)-, -CH₂-N(R_a)-, -N(R_a)-CH₂-,
-C(=O)-N(R_a)-, -N(R_a)-C(=O)-, -N(R_a)-C(=O)-O-, -O-C(=O)-N(R_a)-,
-N(R_a)-C(=O)-N(R_b)-, -N(R_a)-C(=O)-N(R_b)-, -SO₂-N(R_a)- and
-N(R_a)-SO₂-;

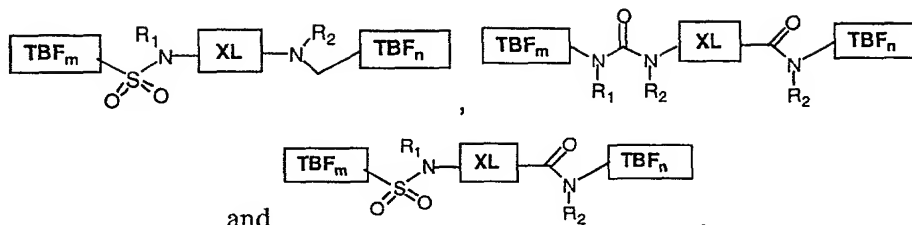
R_a and R_b are independently selected from the group

hydrogen, C₁-C₁₀-alkyl, C₀-C₁₀-alkyl-C₆-C₁₀-aryl, C₆-C₁₀-aryl-C₀-C₁₀-
alkyl, C₀-C₁₀-alkyl-heterocycle-C₀-C₁₀-alkyl, C₁-C₆-alkyl-NH-C₁-C₆-
alkyl, C₀-C₁₀-alkyl-O-C₀-C₁₀-alkyl, C₀-C₁₀-alkyl-C(=O)-C₀-C₁₀-alkyl, C₀-
C₁₀-alkyl-NH-C(=O)-C₀-C₁₀-alkyl, C₀-C₁₀-alkyl-O-C(=O)-C₀-C₁₀-alkyl,
where any alkyl, aryl or heterocycle is optionally substituted with
alkyl, C₁-C₁₀-alkoxy, C₆-C₁₀-aryl, C₆-C₁₀-aryloxy, halo (F, Cl, Br, I),
hydroxy, carboxy, amino, nitro and S(O)_{0.3}.

25. The method of Claim 24 wherein the TBF_m and TBF_n from step (d) each independently bind to the target biological molecule with a K_d of from about 3 mM to about 100 μM.

26. The method of Claim 25 wherein the TBF_m and TBF_n from step (d) each independently bind to the target biological molecule with a K_d of from about 2 mM to about 500 μM.

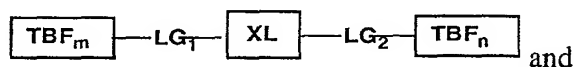
27. The method according to Claim 24, wherein the target biological molecule is a human or human pathogen protein.



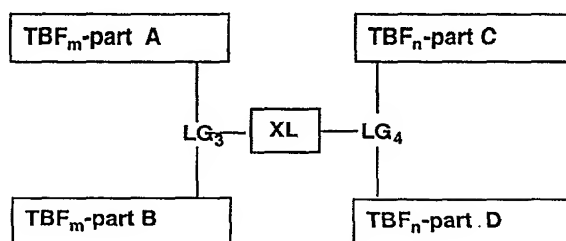
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31. The method of Claim 16 wherein the candidate cross-linked target binding fragments are represented by the formulae:

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where

TBF_m represents a first TBF selected from step (d);

TBF_n represents a second TBF selected from step (d);

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TBF_m-part A and B represent TBF_m from step (d) where each fragment is bonded to a single atom in LG₃;

TBF_n-part C and D represent TBF_n from step (d) where each fragment is bonded to a single atom in LG₄;

XL represents a cross-linker of the formula

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-(C₀-C₂-alkyl-L¹-L²-L³-L⁴-L⁵-C₀-C₂-alkyl)-;

LG₁ and LG₂ are linking groups independently selected from the group

-C(R_a)=N-O-, -O-N=C(R_a)-, -CH₂-N(R_a)-, -N(R_a)-CH₂-, -C(=O)-N(R_a)-, -N(R_a)-C(=O)-, -N(R_a)-C(=O)-O-, -O-C(=O)-N(R_a)-, -N(R_a)-C(=O)-N(R_b)-, -N(R_a)-C(=O)-N(R_b)-, -SO₂-N(R_a)- and -N(R_a)-SO₂-;

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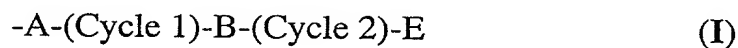
LG₃ and LG₄ are linking groups independently selected from the group

>C=N-O-, -O-N=C<, -CH₂-N<, >N-CH₂-, -C(=O)-N<, >N-C(=O)-, >N-C(=O)-O-, -O-C(=O)-N<, >N-C(=O)-N(R_b)-, -N(R_a)-C(=O)-N<, -SO₂-N< and >N-SO₂-, where < and

> represent two bonds linking TBF-part A, B, C, or D to the single N or C atom in LG₃ or LG₄;

R_a and R_b are independently selected from the group
hydrogen, C₁-C₁₀-alkyl, C₀-C₁₀-alkyl-C₆-C₁₀-aryl, C₆-C₁₀-aryl-C₀-C₁₀-alkyl, C₀-C₁₀-alkyl-
5 heterocycle-C₀-C₁₀-alkyl, C₁-C₆-alkyl-NH-C₁-C₆-alkyl, C₀-C₁₀-alkyl-O-C₀-C₁₀-alkyl, C₀-
C₁₀alkyl-C(=O)-C₀-C₁₀-alkyl, C₀-C₁₀-alkyl-NH-C(=O)-C₀-C₁₀-alkyl, C₀-C₁₀-alkyl-O-
C(=O)-C₀-C₁₀-alkyl, where any alkyl, aryl or heterocycle is optionally substituted
with C₁-C₁₀-alkyl, C₁-C₁₀-alkoxy, C₆-C₁₀-aryl, C₆-C₁₀-aryloxy, halo (F, Cl, Br, I),
hydroxy, carboxy, amino, nitro and S(O)_{0.3};

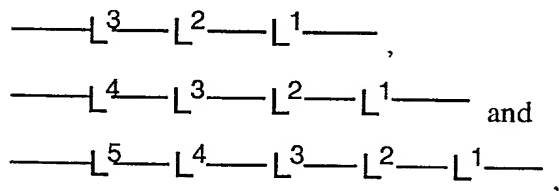
10 TBF_m, TBF_n, TBF_m-part A, TBF_m-part B, TBF_n-part C and TBF_n-part D are
each independently represented by formula I



15 Where

Cycle 1 and Cycle 2 are independently present or absent and are selected from
a mono-, bi-, or tricyclic saturated, unsaturated, or aromatic ring, each ring having 5,
6 or 7 atoms in the ring where the ring atoms are carbon or from 1-4 heteroatoms
selected from; nitrogen, oxygen, and sulfur, and where any sulfur ring atom may
20 optionally be oxidized and any carbon ring atom may form a double bond with O, NRⁿ
and CR¹R^{1'}, each ring nitrogen may be substituted with Rⁿ and any ring carbon may
be substituted with R^d;

25 A and B are independently selected from



30 where:

L¹ is absent or may be selected from oxo (O), S(O)₅, C(=O), C(=N-Rⁿ),
C(=CR¹R^{1'}), C(R¹R^{1'}), C(R¹), C, het, N(Rⁿ) or N;

L^2 is absent or may be selected from oxo (O), $S(O)_s$, $C(=O)$, $C(=N-R^n)$,
 $C(=CR^2R^{2'})$, $C(R^2R^{2'})$, $C(R^2)$, C, het, $N(R^n)$ or N;

L^3 is absent or may be selected from oxo (O), $S(O)_s$, $C(=O)$, $C(=N-R^n)$,
5 $C(=CR^3R^{3'})$, $C(R^3R^{3'})$, $C(R^3)$, C, het, $N(R^n)$ or N;

L^4 is absent or may be selected from oxo (O), $S(O)_s$, $C(=O)$, $C(=N-R^n)$,
 $C(=CR^4R^{4'})$, $C(R^4R^{4'})$, $C(R^4)$, C, NR^n or N; and

10 L^5 is absent or may be selected from oxo (O), $S(O)_s$, $C(=O)$, $C(=N-R^n)$,
 $C(R^5R^{5'})$, $C(=CR^5R^{5'})$, $C(R^5)$, C, NR^n or N;

R^1 , $R^{1'}$, R^2 , $R^{2'}$, R^3 , $R^{3'}$, R^4 , $R^{4'}$, R^5 and $R^{5'}$ each are independently
selected from R^a , $R^{a'}$, R^c and U-Q-V-W; where s is 0-2

15 Optionally, each R^1-R^5 or NR^n together with any other R^1-R^5 or NR^n may
form a mono-, bi-, or tricyclic saturated, unsaturated, or aromatic ring, each ring being
a homo- or heterocycle having 5, 6 or 7 atoms in the ring, optionally each ring
containing 1-4 heteroatoms selected from N, O and S where any ring carbon or sulfur
atom may optionally be oxidized, each ring nitrogen optionally substituted with R^n
20 and each ring carbon optionally substituted with R^d ;

E is $-L^1-L^2-L^3-R^a$;

R^a is selected from the group; hydrogen, halo(F, Cl, Br, I), halo(F, Cl, Br, I)-
25 C_1-C_{11} alkyl, halo(F, Cl, Br, I)- C_1-C_{11} alkoxy, hydroxy- C_1-C_{11} alkyl, cyano,
isocyanate, carboxy- C_1-C_{11} alkyl, amino, C_0-C_{11} alkyl-amino- $(C_1-C_8$ alkyl), C_0 -
 C_{11} alkyl-amino-di- $(C_1-C_8$ alkyl), aminocarbonyl, C_1-C_{11} alkylcarbonylamino,
carboxamido, carbamoyl, carbamoyloxy, formyl, formyloxy, azido, nitro, hydrazide,
30 hydroxamic acid, imidazolyl, ureido, thioureido, thiocyanato, hydroxy, C_1-C_6 alkoxy,
mercapto, sulfonamido, het, phenoxy, phenyl, benzyl, benzyloxy, benzamido, tosyl,
morpholino, morpholinyl, piperazinyl, piperidinyl, pyrrolinyl, imidazolyl and indolyl;

$R^{a'}$ is selected from the group of C_0-C_{10} alkyl-Q- C_0-C_6 alkyl, C_0-C_{10} alkenyl-Q- C_0-C_6 alkyl, C_0-C_{10} alkynyl-Q- C_0-C_6 alkyl, C_3-C_{11} cycloalkyl-Q- C_0-C_6 alkyl, C_3-C_{10} cycloalkenyl-Q- C_0-C_6 alkyl, C_1-C_6 alkyl- C_6-C_{12} aryl-Q- C_0-C_6 alkyl, C_6-C_{10} aryl- C_1-C_6 alkyl-Q- C_0-C_6 alkyl, C_0-C_6 alkyl-het-Q- C_0-C_6 alkyl, C_0-C_6 alkyl-Q-het- C_0-C_6 alkyl, het- C_0-C_6 alkyl-Q- C_0-C_6 alkyl, C_0-C_6 alkyl-Q- C_6-C_{12} aryl and Q- C_1-C_6 alkyl, where any aryl or het is optionally substituted with 1-3 R^d and any alkyl, alkenyl or alkynyl is optionally substituted with 1-3 R^a ;

R^a and $R^{a'}$ may join to form a 3-7 member homocyclic ring substituted with 1-3 R^a ;

R^c is selected from hydrogen and substituted or unsubstituted; amino, O- C_1-C_8 alkyl, amino-(C_1-C_8 alkyl), amino-di-(C_1-C_8 alkyl), C_1-C_{10} alkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, C_3-C_{11} cycloalkyl, C_3-C_{10} cycloalkenyl, C_1-C_6 alkyl- C_6-C_{12} aryl, C_6-C_{10} aryl- C_1-C_6 alkyl, C_1-C_6 alkyl-het, het- C_1-C_6 alkyl, C_6-C_{12} aryl and het, where the substituents on any alkyl, alkenyl or alkynyl are 1-3 R^a and the substituents on any aryl or het are 1-3 R^d ;

R^d is selected from R^h and R^p ;

R^h is selected from the group OH, OCF_3 , OR^c , SR^m , halo(F, Cl, Br, I), CN, isocyanate, NO_2 , CF_3 , C_0-C_6 alkyl- $NR^nR^{n'}$, C_0-C_6 alkyl-C(=O)- $NR^nR^{n'}$, C_0-C_6 alkyl-C(=O)- R^a , C_1-C_8 alkyl, C_1-C_8 alkoxy, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloalkenyl, C_1-C_6 alkyl-phenyl, phenyl- C_1-C_6 alkyl, C_1-C_6 alkyloxycarbonyl, phenyl- C_0-C_6 alkyloxy, C_1-C_6 alkyl-het, het- C_1-C_6 alkyl, SO_2 -het, O- C_6-C_{12} aryl, $SO_2-C_6-C_{12}$ aryl, $SO_2-C_1-C_6$ alkyl and het, where any alkyl, alkenyl or alkynyl may optionally be substituted with 1-3 groups selected from OH, halo(F, Cl, Br, I), nitro, amino and aminocarbonyl, where the substituents on any aryl

or het are 1-2 hydroxy, halo(F, Cl, Br, I), CF_3 , $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ alkoxy, nitro and amino;

R^m is selected from hydrogen, $\text{S-C}_1\text{-C}_6$ alkyl, $\text{C(=O)-C}_1\text{-C}_6$ alkyl, $\text{C(=O)-NR}^n\text{R}^{n'}$, $\text{C}_1\text{-C}_6$ alkyl, halo(F, Cl, Br, I)- $\text{C}_1\text{-C}_6$ alkyl, benzyl and phenyl;

R^n is selected from the group R^c , OH, OCF_3 , OR^o , CN, isocyanate, NH-C(=O)-O-R^c , NH-C(=O)-R^c , NH-C(=O)-NHR^c , $\text{NH-SO}_2\text{-R}^s$, $\text{NH-SO}_2\text{-NH-C(=O)-R}^c$, $\text{NH-C(=O)-NH-SO}_2\text{-R}^s$, C(=O)-O-R^o , C(=O)-R^c , C(=O)-NHR^c , $\text{C(=O)-NH-C(=O)-O-R}^o$, $\text{C(=O)-NH-C(=O)-R}^c$, $\text{C(=O)-NH-SO}_2\text{-R}^s$, $\text{C(=O)-NH-SO}_2\text{-NHR}^c$, $\text{SO}_2\text{-R}^s$, $\text{SO}_2\text{-O-R}^o$, $\text{SO}_2\text{-N(R}^c)_2$, $\text{SO}_2\text{-NH-C(=O)-O-R}^o$, $\text{SO}_2\text{-NH-C(=O)-O-R}^o$ and $\text{SO}_2\text{-NH-C(=O)-R}^c$;

R^o is selected from hydrogen and substituted or unsubstituted $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_0\text{-C}_6$ alkyl- $\text{C}_6\text{-C}_{10}$ aryl, $\text{C}_1\text{-C}_6$ alkylcarbonyl, $\text{C}_2\text{-C}_6$ alkenyl, $\text{C}_2\text{-C}_6$ alkynyl, $\text{C}_3\text{-C}_8$ cycloalkyl and benzoyl, where the substituents on any alkyl are 1-3 R^a and the substituents on any aryl are 1-3 R^p ;

R^p is selected from the group; OH, halo(F, Cl, Br, I), CN, isocyanate, OR^o , SR^m , SOR^o , NO_2 , CF_3 , R^c , $\text{NR}^n\text{R}^{n'}$, $\text{N(R}^n\text{)-C(=O)-O-R}^o$, $\text{N(R}^n\text{)-C(=O)-R}^c$, $\text{C}_0\text{-C}_6$ alkyl- $\text{SO}_2\text{-R}^s$, $\text{C}_0\text{-C}_6$ alkyl- $\text{SO}_2\text{-NR}^n\text{R}^{n'}$, C(=O)-R^c , O-C(=O)-R^c , C(=O)-O-R^o and $\text{C(=O)-NR}^n\text{R}^{n'}$, where the substituents on any alkyl, alkenyl or alkynyl are 1-3 R^a and the substituents on any aryl or het are 1-3 R^d ;

R^s is a substituted or unsubstituted group selected from; $\text{C}_1\text{-C}_8$ alkyl, $\text{C}_2\text{-C}_8$ alkenyl, $\text{C}_2\text{-C}_8$ alkynyl, $\text{C}_3\text{-C}_8$ cycloalkyl, $\text{C}_3\text{-C}_6$ cycloalkenyl, $\text{C}_0\text{-C}_6$ alkyl-phenyl, phenyl- $\text{C}_0\text{-C}_6$ alkyl, $\text{C}_0\text{-C}_6$ alkyl-het and het- $\text{C}_0\text{-C}_6$ alkyl, where the substituents on any

alkyl, alkenyl or alkynyl are 1-3 R^a and the substituents on any aryl or het are 1-3 R^d;

het is any mono-, bi-, or tricyclic saturated, unsaturated, or aromatic ring where at least one ring is a 5-, 6- or 7-membered ring containing from one to four heteroatoms selected from the group nitrogen, oxygen, and sulfur, the 5-membered
5 ring having from 0 to 2 double bonds and the 6- or 7-membered ring having from 0 to 3 double bonds and where any carbon or sulfur atoms in the ring may optionally be oxidized, and where any nitrogen heteroatom may optionally be quaternized and where any ring may contain from 0-3 R^d;

10 U is an optionally substituted bivalent radical selected from the group; C₁-C₆alkyl, C₀-C₆alkyl-Q, C₂-C₆alkenyl-Q, and C₂-C₆alkynyl-Q, where the substituents on any alkyl, alkenyl or alkynyl are 1-3 R^a;

15 Q is absent or is selected from the group; -O-, -S(O)_s-, -SO₂-N(Rⁿ)-, -N(Rⁿ)-, -N(Rⁿ)-C(=O)-, -N(Rⁿ)-C(=O)-O-, -N(Rⁿ)-SO₂-, -C(=O)-, -C(=O)-O-, -het-, -C(=O)-N(Rⁿ)-, -PO(OR^c)O- and -P(O)O-, where s is 0-2 and the heterocyclic rings substituted with 0-3 R^h;

20 V is absent or is an optionally substituted bivalent group selected from C₁-C₆alkyl, C₃-C₈cycloalkyl, C₀-C₆alkyl-C₆-C₁₀aryl, and C₀-C₆alkyl-het, where the substituents on any alkyl are 1-3 R^a and the substituents on any aryl or het are 1-3 R^d;

25 W is selected from the group; hydrogen, -OR^o, -SR^m, -NRⁿR^{n'}, -NH-C(=O)-O-R^o, -NH-C(=O)-NRⁿR^{n'}, -NH-C(=O)-R^c, -NH-SO₂-R^s, -NH-SO₂-NRⁿR^{n'}, -NH-SO₂-NH-C(=O)-R^c, -NH-C(=O)-NH-SO₂-R^s, -C(=O)-NH-C(=O)-O-R^o, -C(=O)-NH-C(=O)-R^c, -C(=O)-NH-C(=O)-NRⁿR^{n'}, -C(=O)-NH-SO₂-R^s, -C(=O)-NH-SO₂-NRⁿR^{n'}, -C(=S)-NRⁿR^{n'}, -SO₂-R^s, -SO₂-O-R^o, -SO₂-NRⁿR^{n'}, -SO₂-NH-C(=O)-O-R^o, -SO₂-NH-C(=O)-NRⁿR^{n'}, -SO₂-NH-C(=O)-R^c, -O-C(=O)-NRⁿR^{n'}, -O-C(=O)-

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R^C , $-O-C(=O)-NH-C(=O)-R^C$, $-O-C(=O)-NH-SO_2-R^S$ and $-O-SO_2-R^S$;

Optionally, TBF_m -part A together with TBF_m -part B and TBF_n -part C together with TBF_n -part D may independently form (Cycle 1) substituted with -B-(Cycle 2)-E..

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31 A compound made by the method of Claim 30.

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